SCIENCE

VOL. 97 FRIDAY, FEBRUARY 12, 1943 No. 2511

SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. MCKEEN CATTELL and published every Friday by

THE SCIENCE PRESS

Lancaster, Pennsylvania

Annual Subscription, $6.00 Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary in the Smithsonian Institution Building, Washington, D. C.

SCIENCE, AND ITS CHANGING SOCIAL ENVIRONMENT[1]

By Professor P. W. BRIDGMAN

HARVARD UNIVERSITY, CAMBRIDGE, MASS.

THE first part of this address dealt with recent work of the author in extending the pressure range attainable in the laboratory. The subject has been similarly treated in the third volume of Science in Progress, published by the Society of Sigma Xi.

And now I will turn from these technical matters, with which I have been personally concerned, to matters of more immediate and vital interest to all of us. In the present world struggle physics has come to occupy a position in the very front line. A large part of the body of physicists has been asked to divert its activities from accustomed channels, and all of us who have been able have rejoiced that the opportunity has been offered and that we can be of service. Because of the obvious importance of the service that physics is rendering, many physicists are anticipating, after the war, a permanent increase of the appreciation of the public for physics, and a great increase in the attractiveness of physics as a profession for our abler young men.

There are, however, other aspects of this rosy future to which I wish to direct your attention. Because of the heavy social impact of the products and techniques resulting from scientific investigation, there is a growing tendency in many quarters to maintain that science, and this of course includes physics, is the servant of society and that all scientific activities should be under complete supervision and control by society or the state. This point of view is finding advocates among scientists themselves. It seems to be growing in favor in some quarters in this country,

[1] Part of the retiring presidential address to the American Physical Society, given at Columbia University, January 23, 1943.

but not yet to the same extent as in Russia, where it is widely accepted, judging by various mass proclamations of Russian scientists published in our press, or in England, where there is an aggressive and articulate group with a similar attitude—the book by Bernal entitled "The Social Function of Science" comes to mind. Indicative of the feeling in some quarters in this country, there is an article in a recent number of the *Popular Science Monthly* which is an extreme example of this point of view. I believe that there is a probability that after the war this feeling will be intensified in proportion to the very success that physicists may have in helping to win the war.

Closely connected with the thesis that scientific activity is a social function is the growing impulse to hold the scientist personally responsible for all the consequences of his discoveries. In all this there is a good deal with which one may sympathize, but I believe that nevertheless an unqualified and unreserved acceptance of the current popular views about the social position of science will result in a false placing of emphasis which in the long run will be harmful both to scientists in their profession, including physicists, and to society as a whole.

The issue is confused by the looseness with which the word "science" is used. Popular usage lumps under the single word "science" all the technological activities of engineering and industrial development, together with those of so-called "pure science." It would clarify matters to reserve the word science for "pure" science. Because a single word is used, there is an impulse to assess a blanket responsibility and to set up blanket controls. Superposed on the confusion arising from verbal looseness there is another less innocent factor. It seems to me that there is often just plain resentment that changes in accustomed routine are so often the outcome of investigations in pure science. Large numbers of the genus homo do not like to be shaken out of an accustomed routine. It is this resentment more than anything else which I believe leads to fastening of "responsibility" on pure scientists. In extreme cases this has even led to the demand for a compulsory moratorium on all scientific investigation.

I think there has been a tendency for scientists in general and physicists in particular to acquiesce too meekly in the implication of social responsibility for their discoveries. The conjuring up of "responsibility" is often only the device of a lazy man to get some one else to do for him something of vital concern to him which he should be doing himself, and scientists in their naiveté have not seen this.

Let us imagine what acceptance of the thesis of responsibility would involve. Perhaps the most fundamental of all the conditions for success in scientific discovery is complete freedom. If the scientist were required to make only those discoveries which could not wilfully be perverted to harmful uses, he would almost certainly feel himself so restricted that he would make no discoveries at all. Furthermore, it is impossible for a physicist or any one else limited by human fallibility to foresee all the consequences of a discovery, much less, to balance all the good consequences against all the bad consequences. Responsibility does not exist when there is no mechanism by which the responsibility can be determined. Neither is there any mechanism by which the physicist can control such consequences of his discoveries as he can foresee. It is society as a whole that is in a position to provide the mechanism of control rather than the individual discoverer, so that it is therefore the responsibility of society to see that discoveries in pure science are properly exploited, not the responsibility of the discoverer. When a physicist makes a new discovery and imparts it to society, he is presenting society with an opportunity, and this opportunity implies responsibility on the part of society.

Society already has available a mechanism of at least partial control in a control of patents and production. Whether an entirely adequate control could be exercised in a framework of a society broken up into separate nationalities as at present may not be easy to decide; certainly the decision and the resultant action is out of the province of the individual scientist.

What is it that makes the "pure" physicist go when he is on the trail of some new idea in his laboratory? The answer is, of course, complex, but I believe that through all the multifariousness runs one simple guiding thread, the craving for understanding. To the extent that the guiding motif of an enterprise is the craving for understanding, to that extent the enterprise may be said to be purely scientific, as distinguished from technological, or utilitarian, or artistic, or political, or what not. The craving for understanding reaches its greatest poignancy only in a few cases, but all of us who are engaged in pure research have it to a certain extent, and it is the vital part of what makes us go. It is not a matter to be argued about, as to whether such a craving has economic or other justification; it is only to be accepted as a fundamental fact about human beings that some of them have developed to a high degree the passion for understanding and a delight in the corresponding activities, just as others have a strongly developed sense of beauty or of conduct. If society is ever going to become anything more than a vicious merry-go-round of circular activity, if ever there are ends in themselves or goods in themselves, then surely the gratification of the craving for understanding is one of them.

To those who have a passion for understanding

society will not be a satisfactory place unless it affords opportunity for the acquiring of understanding, so that to the extent to which the function of society is to make life satisfactory for its members, and it seems to me that this is pretty nearly the whole function of society, one of its responsibilities is the making and providing of adequate scientific opportunity. Society is the servant of science even more and in a more fundamental sense than is science the servant of society. Any control which society exerts over science and invention must be subject to this condition.

Physicists are, I think, even if they give intellectual assent, inclined to be too diffident to insist on all the implications of this conclusion. Many of us find it uncongenial to thrust ourselves forward and to insist on the service owed us by society, particularly at the present. We have a feeling that we should not confuse the issue of winning the war by insisting on matters of obvious personal concern at a time when the very existence of the society to which we are accustomed is threatened. I would urge that on the contrary now is the time more than ever to insist that society must conform to the pattern of service to science. What are we fighting for anyway? After we have scavenged the world of the blight of totalitarianism, what are our long-range objectives? Have we nothing eventually in view more admirable than the abolition of want and the securing of comfort for everyone, ends which at present bulk so large in our programs? Will we be permanently satisfied with these, or will something more be necessary to give dignity and worth to human activity?

In urging the claims of science and scientists on society we may fortify ourselves by reflecting that we are not urging society to give without return. The exercise of the mind and the acquiring of understanding is after all not an ignoble human activity. In more idealistic phraseology it is sometimes described as the pursuit of truth. One might even argue that it is the one human activity which distinguishes us most from the brutes; certainly it is the one in which there is the greatest room for future development and in which we have most failed up to now to realize our full potentialities. In the long run society is a better place for every one when there is intellectual freedom and encouragement and flourishing activity in pure science. It does not put much of a strain on other social mechanisms to have scientific activity going on, nor are we an obtrusive class. We work hard and like it; the pursuit of personal comfort or even happiness is not a particularly compelling motive with us; there is a certain disinterested impersonality in our striving which has on occasion been commended. We do not ask for much in comparison with what we give: freedom and leisure to do our work and decent security for the future. Many of us already have been more or less fortunate in these respects, and some of us already have been living under conditions which approach the millennium according to our simple standards. But it seems to me that the prospect is becoming less bright. Not many people like to use their minds, and there is always some spontaneous hostility of those who do not like to think toward those who do. For years before the war there were signs of a growing anti-intellectual sentiment, which I believe is now becoming visibly intensified with the passions and emotions always associated with war. It seems to me that scientists are curiously obtuse as to the social conditions which make possible their existence as a class. It is by no means a certainty that society will so evolve that the individual will be allowed to engage in independent intellectual activity. The danger of such an evolution increases with the growing command by society of techniques assuring a satisfactory degree of common ease and comfort. Society may well come to feel that the scientist has not enough more to give it in the way of material benefits to justify keeping him. If society is ever going to become a place in which intellectual activity is encouraged and intellectual ability prized, those of us who like to think have got to fight for it. If we do not take action in our own behalf, no one else will do it for us. And we must do it now because social institutions are changing so rapidly that after the war it may be too late. Judging by the one criterion of greatest significance in this country, economic position, there is no doubt that the changes now taking place are leading to a worsening of the position of those who like to think as contrasted with those who do not. When we contemplate all the pressure groups insistent only on their own advantage, we need not be diffident in striving for an even greater recognition than in the past of the social importance of intellectual activity, and of the importance of stimulating such ability by commensurate rewards.

A distorted conception of democracy is forming under stress of the war, a conception which urges the equal right of every one to share the goods of society irrespective of what he gives back to society. The conception of democracy which was implicit in the old fashion "American ideal" seems to me more admirable. According to this conception democracy meant equal opportunity for ability, no matter how humble its origin, to rise to its natural level. So far as capitalism was discussed at all, it was justified, at least in theory and in spite of its defects, because it incidentally provided a machinery by which special service received special reward. It was not considered that a society was either ignoble or undemocratic that gave special reward for special service. Nor was the individual who consented to receive special reward for special service considered to have debased himself. It was felt

that society need not grudge to act to its own advantage because it was also for the advantage of the individual; society did not resent the individual of exceptional abilities but took pride in him. It seems to me that a certain crabbed and ungenerous spirit of envy and resentment against unusual ability is growing; this is underlined by recent events. To me there is something dead wrong with a social philosophy that attempts to set *any* upper limit to the value of the contribution which a man of unusual ability can make to his society, particularly in time of war. In the name of democracy our ideals are becoming less democratic. A partial explanation is doubtless to be found in industrial and capitalistic abuses. But an explanation does not constitute a justification.

We, who are perhaps more vitally concerned than any other group, have thus far failed to take steps to ensure that the economically altered society of the future shall retain those essential features that once inspired our democratic vision. Our conviction has not been strong enough that a society is a good society in which intellectual ability is prized and rewarded. We are passively accepting a change in the economic system by which the relative position of all intellectual workers, including the scientist, is being definitely debased, and in which assurances and commitments made by society in the past are being needlessly scrapped. This applies with particular force to the private universities and to the workers in them. We are not fighting against these things ourselves, and we in the universities are not insisting that our university and educational administrators fight for them for us.

What are we going to do about it? In the first place, we are not going on strike, but those of us who are in the position will continue to work as hard as we can to develop all the devices in the power of our ingenuity or to make what other special contributions we can to destroy totalitarianism and all that it implies. Neither, I think, will scientists attempt to organize themselves into a pressure group to try to mold society to their pattern. Even if it were not ludicrous for so small a minority to think of making such an attempt, we would find such an attempt distasteful at a time when so many of our young men are being called on to make extreme sacrifices. And even if not distasteful, who could find time to devote to such an attempt when we are all so busy with immediate things? But it would be stupid not to take time to at least see what the situation is, and once having seen it, it will be possible to do many things incidentally without slackening in our other efforts. Merely by letting it be known that we are aware of the situation we may accomplish something. From the long range point of view our job is primarily one of education. We should avail ourselves of every opportunity and even go out of our way to make opportunity to let our conviction be known that a society is in the long run the best society in which those who have the ability are given every opportunity and inducement to practice the pursuit of truth and of understanding. We must hold up intellectual power and accomplishment to the admiration and emulation of our young and stimulate their pleasure in intellectual activity. Our educational programs must be revised if necessary to give this emphasis. We must teach our young a social philosophy which recognizes that society is a means and not an end, and we must give them a technique by which they can discover those ends which they can accept with intellectual integrity as making society worth while. If we do not do these things, we are in danger of finding when this struggle is over that we have been fighting for a lifeless husk; if we do them we will be playing our part in molding a public opinion which will create the society of our vision.

DIGITALIS AND SOME OF ITS DERIVATIVES. II

By Dr. HARRY GOLD

DEPARTMENT OF PHARMACOLOGY, CORNELL UNIVERSITY MEDICAL COLLEGE

(*Continued from page 129*)

One of the results of these studies was to show that a similar number of units determined on the frog (U.S.P. XI units) produced widely different effects, while the degree of effect paralleled the number of units determined on the cat. The frog, therefore, appears not to be a suitable animal for the standardization of digitalis preparations that are to be used in man. When the frog and the cat method give different answers in a comparison of specimens of digitalis, that obtained with the cat method is more nearly applicable to humans.

The cat method has now been adopted as the official method of assay in the Twelfth Revision of the U. S. Pharmacopeia. It is to be expected that in the future the potency of digitalis preparations of commerce will be more uniform.

There are certain objections to the cat method as well, since the technique involves intravenous injection, and in that way it fails to distinguish between absorbable and non-absorbable material. This is a matter of some importance, since digitalis is most commonly administered orally in man.

There is abundant reason for the belief that the potency of a specimen of digitalis or a glycoside which is to be used in man should be assayed directly on man.

A method for the assay of digitalis directly on humans has been developed.[21]

Fig. 4 illustrates the technique of an assay in one human subject. The average of a series of such cases represents a complete assay. The essential principles

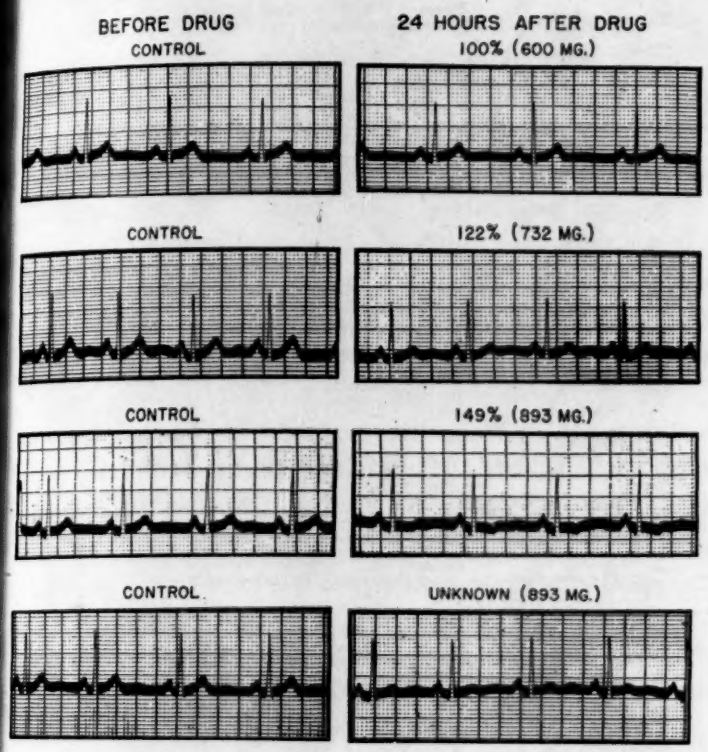

FIG. 4. Assay of digitalis directly on man. Subjects are selected in whom the T-wave is a sensitive indicator of digitalis action. The response of the T-wave is calibrated by graded doses of the standard (U.S.P. Reference Standard) given at one-month intervals. In the above case, T-wave changes clearly differentiate 22 per cent. differences in doses of the standard. Note that 893 mg of the unknown produce an effect between that of 732 and 893 mg of the standard. Hence the unknown has a potency approximating 812 mg or 91 per cent. of the standard.

of bioassay are applied in this method. The sensitivity of the test subject is first determined. A dosage-response curve is established for each case, and the unknown specimen is compared with a standard within the range of the points on this curve.

The reproducibility of results with the human assay, if it is carried out on a properly selected group of human subjects and the technique is followed in all its details, is quite remarkable. We have had an opportunity to assay one specimen of digitalis four times, once in the form of tablets, another time in the form of capsules of the leaf, then in the form of a tincture made from the leaf, and another time in the form of a second tincture made from that leaf. These assays were made on different groups of patients. In humans, the first proved to be 82 per cent. of the potency of the Reference Standard, the second 77.8 per cent., the third 86.9 per cent. and the fourth 77.5 per cent. The average for the four assays of the same specimen indicated that that digitalis was 81 per cent. of the standard, with a maximum deviation from the lowest to the highest figure of less than 10 per cent. Such reliability is not often obtained by animal assay methods.

It is, of course, the hope that one day digitalis materials in general use will be sufficiently pure and constant so that their identity will be ascertained by more precise physical and chemical methods. In that case, we shall dispense with bioassay. But until then the human assay provides the final decision in the matter of the potency of digitalis. To be sure, the human method of assay is not as convenient as the animal methods. The subjects are not as accessible to as many workers. When the importance of human assay is better recognized, however, the apparent disadvantage may be turned to good use in that fewer batches of digitalis may be subjected to assay. The pooling of digitalis into larger units for assay would in itself go a long way toward establishing uniform potency among this group of drugs.

Closely related to the matter of bioassay of digitalis is the problem of digitalis deterioration. After a tincture is stored for about 3 or 4 months it may lose as much as 50 per cent. of its previous potency as revealed by the frog test. But, by the cat test, the tincture usually retains its previous strength. The explanation of this is not clear. It may be that, upon standing, the potent glycosides in the tincture undergo some form of physical change which alters their absorption from the lymph sac of the frog, although in this form it retains its full potency when injected intravenously in cats. Tests with a very old tincture which had "deteriorated" to about one half its strength by the frog method showed full strength in humans. These tests were made by the method illustrated in Fig. 3.

There is considerable controversy concerning the question whether or not the quality of action of different digitalis glycosides is the same. If one material fails to produce satisfactory therapeutic effects, assuming that it has been absorbed and that the dose has been large enough, is it likely that some other preparation of digitalis will accomplish more? That question arises particularly in connection with the treatment of patients in advanced heart failure whose response to digitalis materials is often incomplete or equivocal. From the results of some of the more recent experiments with heart-lung preparations,[22] the conclusion has been drawn that the margin between therapeutic and toxic effects on the heart is much wider for some than for other glycosides. The existing

[21] H. Gold, McK. Cattell, H. L. Otto, N. T. Kwit and M. Kramer, *Jour. Pharmacol. and Exp. Therap.*, 75: 196, 1942.

[22] G. K. Moe and M. B. Visscher, *Jour. Pharmacol. and Exp. Therap.*, 64: 65, 1938.

evidence for this view leaves much to be desired. No significant differences in the margin between toxic and therapeutic doses of a wide variety of digitalis glycosides could be observed in the experiments on the mammalian papillary muscle.[23] The subject has also been studied in man. In these experiments the ratio of therapeutic to toxic dose was measured by the incidence of toxic symptoms when the therapeutic dose was doubled. It was found that with this as a criterion, the spread between the therapeutic and toxic dose for the preparations studied, digitalis, Lanatoside-C and Digitoxin, were substantially the same. The view that strophanthin by intravenous injection produces effects which can not be obtained with digitalis has been popular in the European literature for many years, and has recently been revived in this country. No good evidence exists that this is so, provided suitable measures have been taken to insure that adequate amounts of the glycosides have reached the circulation. We have compared several digitalis materials by intravenous injection, giving the same number of cat units of each in a single dose: ouabain, Lanatoside-C or Cedilanid, Digitoxin and the mixture of glycosides found in digitalis in the form of Digifoline (Ciba). A single injection of 3 cat units of each produces approximately the same result. The effects appear within a matter of minutes, are fully developed within about 1 to 2 hours, and the degree of the effect when fully developed is substantially the same. These experiments were made in patients with auricular fibrillation confined to bed in the hospital, after a long control period, in much the same way as those described in Fig. 3.

One of the most significant pharmacological properties with respect to which digitalis materials show wide differences is that of absorption from the gastrointestinal tract. We have studied this factor in man by the comparison of the amounts necessary to produce the same effect by oral and intravenous administration. all comparisons being made in one and the same subject. The results show that, while digitalis and its tincture are the most absorbable among the crude members of the digitalis group, not more than about one fifth of the potent materials in digitalis plays a part in the therapeutic effects of the drug when administered orally. The rest is chiefly non-absorbable material. An intravenous dose of 3 to 5 cat units produces the same effect as 15 to 20 cat units given orally in the same patient.

The purification of digitalis has often resulted in little improvement in absorption (Fig. 5).[24] The purified principles are in some instances more poorly absorbed than digitalis leaf, as shown by the wide spread between the intravenous and the oral dose necessary for an equal effect. The most outstanding exception is Digitoxin (Digitaline Nativelle). We

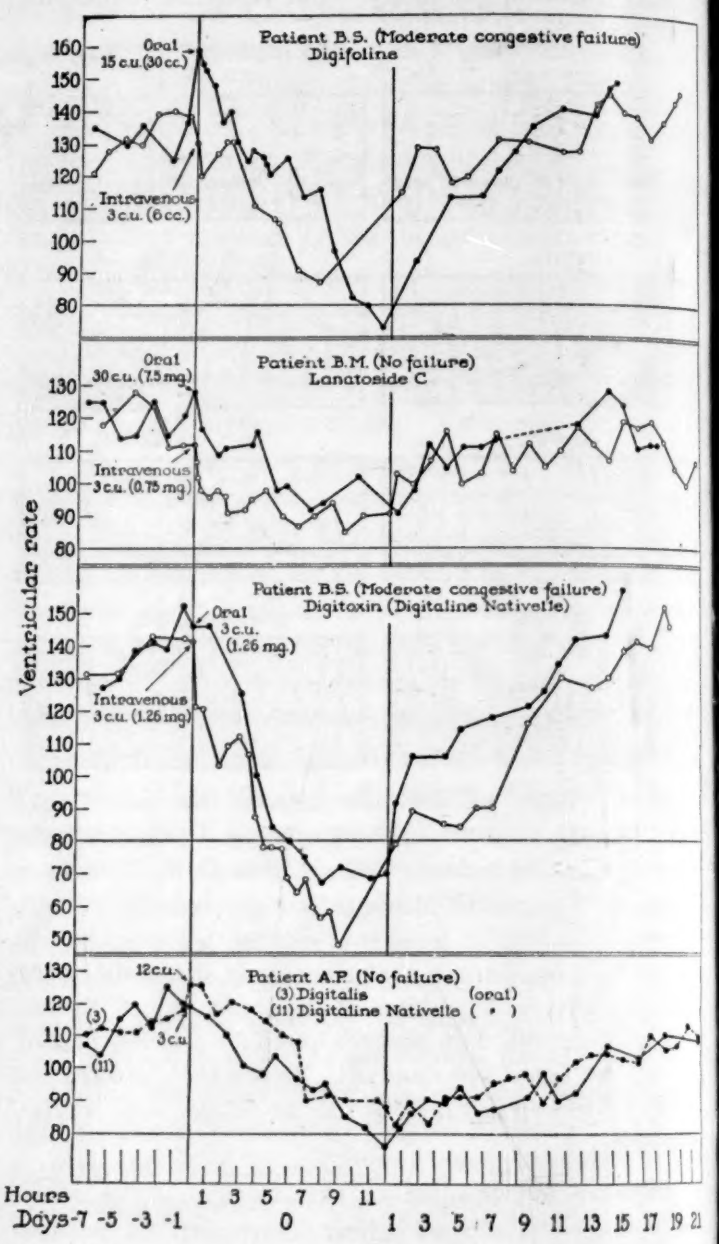

FIG. 5. These patients had auricular fibrillation and were confined to bed. The points on the curves were obtained in the same way as those in Fig. 3. Note that the ratio of oral to intravenous dosage for Digifoline is 5:1, for Lanatoside-C 10:1, for Digitoxin 1:1. Although these ratios vary somewhat from one experiment to another, they represent the usual relationships for these preparations.

have recently subjected this material to more intensive study in animals and man. It possesses a property quite unique for a digitalis body, that of complete absorption from the gastrointestinal tract. A given amount produces the same intensity of effect whether given orally or intravenously. The full digitalizing doses by the two routes in man are practically identical, namely, 1.25 mg or a total of 3 cat units. It is absorbed directly through the wall of the stomach.

These properties have been put to use in an im-

[23] McK. Cattell and H. Gold, *Jour. Pharmacol. and Exp. Therap.*, 71: 114, 1941.

[24] Differences in elimination and destruction within the intestinal tract may play a minor part in the differences attributed to absorption.

proved technique for the treatment of heart failure. In the case of digitalis, it is customary to take a day or two or longer to induce the full effects. The full dose, whatever it is estimated to be, 1 gram or 1.5 grams for a given individual, is divided into 4 or 5 fractions and given at 6- or 8-hour intervals. It is not essential to give it all at one time, since the average patient with heart failure is not *in extremis*, and little is lost by taking 2 or 3 days rather than 6 to 8 hours to induce the full effects. However, the chief reason for the divided doses is the fact that from a single full dose given at one time poisoning may result in the more susceptible individuals. Since varying susceptibility as measured by oral doses includes the factor of varying absorption, it was considered that Digitoxin (Digitaline Nativelle), which is rapidly and, for practical purposes, completely absorbed from the gastrointestinal tract, might provide a means of safe full digitalization by a single dose method. This was found to be the case. The average full digitalizing dose of 3 cat units (1.25 mg) may be given at one time to the patient with heart failure who has not recently received digitalis. It induces the full effects within a period of about 6 hours, sometimes more quickly. With this material there is provided a safe routine procedure of oral digitalization within a few hours rather than in days, as is the case with the customary technique by which digitalis is used.

Digitalis leaf or the tincture can not take the place of Digitoxin in the single dose method of digitalization. A therapeutically equivalent dose represents about 15 cat units, and this causes nausea and/or vomiting in 1 out of every 5 patients within less than two hours, due to a local irritant action, although the local emetic action of digitalis is rarely seen when the full amount is given in a series of small fractions. On the other hand, in the case of Digitoxin, a local emetic action is rarely seen even after the single full digitalizing dose, because the total glycoside for the full effects amounts to only 1.25 mg.

A sharp distinction needs to be drawn between the local and the systemic emetic action of the digitalis bodies. All the digitalis glycosides exert both types of action. We have experiments, however, with various materials such as the glycosides of squill, extracts of digitalis purpurea and of digitalis lanata, and ouabain, which indicate that it requires between 5 and 10 mg of the glycosides, sometimes more, to produce nausea and vomiting by the local action in the gastrointestinal tract. Such an action is therefore to be expected in the case of digitalis materials in which so much of the glycoside is necessary for the full therapeutic effects. It is not likely to occur with those materials of which, by reason of their high potency and completeness of absorption, smaller total amounts of glycosides suffice for full therapeutic effects.

OBITUARY

FRANZ CARL SCHMELKES

1899–1942

HIS colleagues in chemistry, his many friends in the field of medicine and his associates in the industry were shocked to learn of the death of Franz C. Schmelkes. After reiewing his last manuscript he left his office on the evening of December 11, and did not return to his desk the next morning as expected. He had succumbed to a heart attack during the night. This marked the end of a life unusually productive in the realm of science and its industrial applications.

He was born in Prague in 1899, and received his training in organic chemistry at the Carl-Ferdinand University in the same city. He obtained the degree of doctor of philosophy in 1922. For four years he worked in Hanover, Germany, at the Continental Rubber Company and in 1925 he came to the United States. Before joining the staff of the Research Laboratories of Wallace and Tiernan Company, he was associated with the Dovan Chemical Company in Newark, and the Davis Emergency Equipment Company in Hoboken, N. J. For about a decade he had been the assistant director of research of Wallace and Tiernan Products, Inc.

His first major contribution was the synthesis of N,N′-dichloroazodicarbonamidine, a chloramine which is now widely used as a disinfectant. He often referred to this chlorine compound as a "chlorine reservoir" and he felt that its success as a disinfectant is not only due to the slow release of chlorine but also to a quasi-selective action towards bacteria. He and his associates investigated its disinfecting properties extensively, and he collaborated closely with those physicians who used it clinically. His work with this disinfectant brought him in close contact with medicine; and in a short time he acquired an amazing knowledge in all branches of this science. He applied his knowledge of organic chemistry with great ingenuity to problems of therapeutics and usually attacked these problems on a broad front and on the basis of a rather general working hypothesis.

Stimulated by some evidence in the literature indicating that isosteric compounds are similar in their biological activity, he synthesized a group of isosteric compounds and investigated them pharmacologically. One of these was a thiamine analogue; another, a nicotinic acid analogue. Both compounds showed a considerable and specific vitamin activity.

In recent years he was intensely interested in the mechanism of sulfonamide action. He investigated the effect of the hydrogen ion concentration on the activity of sulfonamides *in vitro* and found an interesting correlation between the acidic dissociation constants of the sulfonamides and the effect of the pH upon their activity. The conclusion could be drawn from the data collected by him and his associates that the anionic form of sulfonamide is a great deal more active than the undissociated sulfonamide molecule and that the activity of the latter is negligible in comparison. The activity of sulfanilamide, in particular, was found to be greatly enhanced by the adjustment of the pH. The activity of sulfanilamide at the optimal pH, although not directly measured, was calculated to be greater than that of any other known sulfonamide. The practical conclusion was drawn that the local chemotherapy for wound infections should be carried out with sulfanilamide and a buffer.

He was a strong advocate of the theory that sulfonamide activity is due to the blocking of the *p*-aminobenzoic acid receptor in an enzyme system, and on the basis of this theory he and his associates synthesized various *p*-aminobenzoic acid derivatives, some of which showed a typical sulfonamide activity, that is, anti-bacterial activity which could be reversed by *p*-aminobenzoic acid. He realized the practical importance of inactivating the *p*-aminobenzoic acid which is the antagonist of sulfonamide in local chemotherapy and he worked intensely on the study of the use of N,N′-dichloroazodicarbonamidine for this purpose.

Since Pearl Harbor, he has concentrated all his efforts on the medical aspects of the war. He developed an ingenious treatment of burns, using a membrane which contains buffered sulfanilamide as a chemotherapeutic agent.

Franz Schmelkes' interest was not limited to science but embraced political, social and economic problems. He had beliefs and convictions for which he was always ready to fight. His greater interest was in his fellowmen, many of whom he helped when in need. He was a member of many scientific societies and was popular at the Chemists' Club. One of his favorite sports was golf. His guiding spirit and stimulating influence will long survive among his friends and associates who will miss him greatly.

L. REINER

RECENT DEATHS

DR. EDGAR ALLEN, professor of anatomy and head of the department at the Yale University School of Medicine, died on February 3 at the age of fifty years.

DR. EARLE RAYMOND HEDRICK, a member of the faculty of the Brown University Graduate School in Advanced Instruction and Research in Mechanics, formerly vice-president of the University of California at Los Angeles, died on February 3 at the age of sixty-six years.

DR. LEONARD MAGRUDER PASSANO, professor emeritus of mathematics of the Massachusetts Institute of Technology, died on January 30 in his seventy-seventh year.

DR. J. FRANK FRASER, consulting dermatologist at the Memorial Hospital for the Treatment of Cancer and Allied Diseases and other New York hospitals, has died at the age of seventy-two years.

MISS CAROLINE HARRISON, better known to her friends as "Carrie Harrison," died at her home in Washington, D. C., on about January 19. She entered the government service in the division of botany of the Department of Agriculture in 1887. The division later became a part of the Bureau of Plant Industry. Miss Harrison gave special attention to tannin-bearing plants. She was an enthusiastic rosarian, and was an active member of the American Rose Society up to the time of her death. She retired from government service in April, 1926.—F.A.W.

SCIENTIFIC EVENTS

THE BRITISH NEW YEAR HONORS LIST[1]

THE following names of scientific men and others associated with scientific work appear in the British New Year honors list:

Baron: Sir Charles Wilson, president of the Royal College of Physicians.

Baronet: W. M. Goodenough, chairman of the Nuffield Trust for the University Medical School, Oxford.

G.B.E.: Sir Henry Dale, lately director of the National Institute for Medical Research, president of the Royal Society.

[1] From *Nature*.

K.C.B.: Sir Wilson Jameson, chief medical officer, Ministry of Health and Board of Education.

Knights: Professor J. H. Clapham, president of the British Academy; Professor F. Clarke, professor of education, University of London; Dr. A. C. G. Egerton, professor of chemical technology, Imperial College of Science and Technology, and joint secretary of the Royal Society; Jhanendra Chandra Ghosh, director of the Indian Institute of Science, Bangalore; S. H. Howard, inspector-general of forests and president of the Forest Research Institute, Dehra Dun; Pestonji Rustom Masani, lately vice-chancellor of the University of Bombay; W. A. Stanier, chief mechan-

ical engineer L.M.S. Railway and scientific adviser to the Minister of Production; Brigadier E. O. Wheeler, surveyor-general of India; J. Wright, chief engineer, Central Electricity Board.

C.M.G.: D. Yates, a leading metallurgist of South Australia.

C.I.E.: Bhagavathulu Viswanath, officiating director, Imperial Agricultural Research Institute, New Delhi; R. A. MacGregor, chief metallurgist, Department of Supply, Calcutta.

C.B.E.: Dr. W. R. Aykroyd, director of nutritional research, Coonoor; E. Barnard, director of food investigation, Department of Scientific and Industrial Research; R. Gushue, chairman of the Fisheries Board, Newfoundland; E. H. E. Havelock, administrative secretary of the Agricultural Research Council and Secretary of the Development Commission.

THE TINGO MARIA EXPERIMENT STATION

A SPECIAL correspondent in Lima, Peru, of *The New York Times* reports that Dr. Benjamin J. Birdsall, of the Office of Foreign Agricultural Relations of the U. S. Department of Agriculture, has been appointed director of the agricultural experiment station at Tingo Maria. He arrived in Peru at the end of July. The United States, through the Department of Agriculture, in cooperation with the State Department is contributing financial and technical aid, while Peru is contributing land, buildings and other facilities.

The station at Tingo Maria is one of a series of agricultural experiment stations being established throughout the American tropics designed to assist and encourage the production on a large scale of rubber, quinine and other products formerly obtained from the Far East. As assistants, Dr. Birdsall has William Wickline, formerly in the U. S. Government service in entomology and plant quarantine work, and Rolland Lorenz, a rubber expert, formerly with the Firestone Company in Africa. In 1940 Dr. Lorenz was a member of one of the U. S. missions which made a survey of the rubber possibilities of tropical America. The American group at Tingo Maria works in direct cooperation with Pedro Recavarren, director of forest lands and colonization. Pedro Beltran is serving as government aide in the organization of the undertaking.

The experiment station at Tingo Maria, which is situated on the Huallaga River on the eastern slopes of the Andes, according to *The New York Times* correspondent, will consist of three main buildings and twenty residences all constructed of brick with enternite roofing. The principal building or "head house plant," as it is called, will comprise the main laboratories and greenhouses. In addition there will be an administration building with offices and library, and a dormitory or club-house for single men. The cost will be in excess of $160,000, and the building program is expected to take two years. A plant for fabricating the brick is now being completed at Tingo Maria. The grounds of the station cover five hectares, along the Central Highway of Peru, within the urban limits of the town of Tingo Maria. Additional land is being acquired for the experimental work.

GIFTS RECEIVED BY THE UNIVERSITY OF WISCONSIN

AT a recent meeting of the Board of Regents of the University of Wisconsin, it was announced that gifts had been received amounting to $38,811.

The sum of $5,500 was given by Lever Brothers Company, Mass., for the continuation of an industrial fellowship in biochemistry, under the supervision of Professor Harry Steenbock. A grant was made also by the Wisconsin Alumni Research Foundation for the support of the general research program of Professor Steenbock.

Federal aid amounting to $4,720 was accepted for the Public Health Nursing program of study for the training of twenty-two public health nursing students.

In addition to a number of smaller gifts, $1,000 was received from the State Rural High Schools Committee for a field study in rural community education by Clarence E. Ragsdale, associate professor of education; $1,000 from the National Canners Association, Washington, D. C., an addition to the original grant of $3,000 for an industrial fellowship in biochemistry; $1,500 from General Mills, Inc., Minneapolis, for the continuation of an industrial fellowship in the department of biochemistry, under the supervision of Professor C. A. Elvehjem; $1,200 from Eli Lilly and Company, Indianapolis, for the renewal of an industrial fellowship in the department of biochemistry, also under the supervision of Professor Elvehjem, and $3,000 from the National Canners Association for the establishment of an industrial fellowship in the department of biochemistry under the supervision of Professor Elvehjem and Professor F. M. Strong; $1,000 from the Oscar Mayer Company, Madison, for the establishment of an industrial fellowship in the department of animal husbandry under the supervision of Professor A. E. Darlow; for the support of scholarships of $75 each for farm boys, $750 was given by Oneida Farms, Inc., and $300 by the Oscar Mayer Company.

Five hundred dollars was received from the Wisconsin Alumni Research Foundation, as an addition to the $5,000 grant for an industrial fellowship in biochemistry, under the direction of Professor Karl Paul Link; and $2,000 from the Upjohn Company, Kalamazoo, for the establishment of a research assistantship in the department of pharmacology and toxicology, under the supervision of Professor A. L. Tatum.

WAR SERVICES OF THE UNIVERSITY OF ILLINOIS

THE extent to which the Federal Government has called upon the University of Illinois for special war services is reported by Comptroller Lloyd Morey, who states that special war contracts with the university involve the sum of $2,383,694.

They are being carried on in addition to the regular work of instructing 11,495 students, of whom 4,700 are in the Reserve Officers Training Corps and 2,915 in the enlisted reserves; to the regular research activity, much of which has war value; and to the release of 485 staff members on leave for military and war work.

The largest special activity in terms of persons involved is the engineering, science and management war-training program being carried on in fifty-two Illinois industrial areas by the Division of University Extension for the U. S. Office of Education; 15,928 war workers have been trained or are now in classes. For this training program the university has received $955,798.

The U. S. Navy has established at the university a training station for 2,000 signalmen, diesel officers, diesel engineers, and cooks and bakers. For housing, laboratories, classrooms, meals and other services, and for necessary changes in the buildings to meet Navy needs, the Federal Government has contracted to pay $963,725, and has paid $665,000 up to January 21.

The university has twenty-nine research contracts with various Federal agencies involving the sum of $439,354 for work in the physical sciences, chemistry, medicine and engineering. Several other research projects are being planned and may soon be under way. From the Civil Aeronautics Authority $24,817 has been paid for the training of 270 student pilots.

RARE CHEMICALS

THE following chemicals are wanted by the National Registry of Rare Chemicals, Armour Research Foundation, 33rd, Dearborn and Federal Streets, Chicago, Ill.:

1. Na Hyposulfate
2. Adonitol
3. Phosphoglyceric aldehyde
4. Hydroxypyruvic acid
5. Quinic acid
6. Thionalide (Thioglycolic Acid-B-Amino Naphthalide)
7. Dimethyl Acetylene
8. Protocatechuic Acid
9. Tribromo Caffein
10. Trimethyl Borine Amine
11. Indican
12. 2-Desoxyribose
13. a-Tetralone
14. Cyclopentadiene Carboxylic Acid
15. Triphosgene
16. Methyl vinyl ketone
17. Boron trichloride
18. Ethylene diamino tetra acetic acid
19. Nitrile triacetic acid
20. Organic compounds of selenium

THE RESEARCH AWARD OF ELI LILLY AND COMPANY

THE annual meeting for 1942 of the Society of American Bacteriologists originally scheduled for December 28, 29 and 30 at Columbus, Ohio, was cancelled at the request of the Office of Defense Transportation. This necessitated the postponing of the research award given by Eli Lilly and Company. It was presented at a joint meeting of the Iowa State College Branch of the Society of Sigma Xi and the North Central Branch of the Society of American Bacteriologists, on January 28, to Dr. Harland G. Wood.

The annual research award of $1,000 and a bronze medal have been offered by Eli Lilly and Company to a young man or woman, under thirty-five years of age, who has made outstanding contributions to knowledge in the fields of bacteriology or immunology while conducting investigative work in a non-commercial research or educational institution in the United States or Canada. This award is being made to stimulate research activity in young people and to recognize meritorious achievement and promise at an early stage in their careers. The recipient is chosen by an award committee composed of members of the Society of American Bacteriologists, the American Association of Immunologists and the American Society for Experimental Pathology. This year an unusually large number of nominees with impressive records of accomplishment was submitted to the committee. From them, the committee has selected as the 1942 recipient of the award Dr. Harland G. Wood. The citation reads:

> The award is made on the basis of Dr. Wood's outstanding contributions to bacterial physiology. In this work it was shown that typical heterotrophic bacteria utilize carbon dioxide in their metabolism and that the carbon dioxide is bound to other carbon compounds playing an important part in cell physiology. The bound carbon dioxide was traced to show its location in the resulting compounds and its important role in respiration. The scope and significance of these findings was broadened materially by the further demonstration that this change is not limited to microorganisms but applies to higher forms of life.
>
> This work is significant as a contribution to fundamental life processes. It shows that the distinction between autotrophic and heterotrophic microorganisms can not be drawn as sharply as formerly believed. It indicates a starting point for further study of autotrophic carbon dioxide utilization and photosynthesis. It is an important contribution to the study of cell respiration.

It possesses broad significance as another link in the chain of accumulating evidence indicating general similarity of many metabolic processes in diverse forms of life.

Dr. Wood's first contribution to this field was made in 1935, and he is one of the pioneers in opening a new avenue of study in bacterial physiology. Throughout these investigations Dr. Wood has shown himself to be a skilful and versatile investigator bringing to the solution of his problem methods and technics from several fields of scientific endeavor.

COMMITTEE ON APPLIED MATHEMATICAL STATISTICS OF THE NATIONAL RESEARCH COUNCIL

THE Committee on Applied Mathematical Statistics of the National Research Council and its subcommittees will be concerned with problems involving personnel and organization, research and production. The services which it is prepared to render are consultation, assistance in the organization and direction of special research projects and the preparation of necessary manuals on statistical techniques.

At present, the committee is particularly interested in the use that industries and government agencies may make of statistical quality control in production. Those industries and government agencies that have been making use of statistical quality control find that it has been possible to reduce the quantity of defective material, the amount of necessary inspection, reduce the tolerance range where necessary in order to save material, and attain assurance that the quality of material that can not be inspected one hundred per cent. because of the destructive nature of the test will meet the standard specified. The general oversight of this phase of the work of the committee is in charge of Dr. Walter Shewhart.

The membership of the committee and subcommittees is as follows:

Committee on Applied Mathematical Statistics:

Luther P. Eisenhart, *Chairman.* (Chairman of the Division of Physical Sciences.)

Edward U. Condon, Westinghouse Electric and Manufacturing Company.

Lowell J. Reed, School of Hygiene and Public Health, the Johns Hopkins University.

C. F. Roos, Institute of Applied Econometrics, Inc., 500 Fifth Avenue, New York City.

W. A. Shewhart, Bell Telephone Laboratories, Incorporated.

Hugh M. Smallwood, United States Rubber Company, Eau Claire, Wisconsin.

John M. Stalnaker, Princeton University.

S. S. Wilks, Princeton University.

Sewall Wright, Department of Genetics, the University of Chicago.

Liaison members:

Victor Perlo, Office of Price Administration.

Commander Lybrand Smith (retired), Navy Department.

Herbert Stein, War Production Board.

Lieutenant Colonel John D. Witten, War Department.

Subcommittee on Mathematical Statistics:

S. S. Wilks, *Chairman.*

Churchill Eisenhart, University of Wisconsin.

W. Edwards Deming, Bureau of the Census.

Subcommittee on Biology:

Sewall Wright, *Chairman.*

Chester I. Bliss, Yale University.

John W. Gowen, Iowa State College.

George W. Snedecor, Iowa State College.

Subcommittee on Chemistry:

Hugh M. Smallwood, *Chairman.*

Warren F. Busse, B. F. Goodrich Company, Akron, Ohio.

Henry Eyring, Princeton University.

Oscar K. Rice, University of North Carolina.

Felix L. Yerzley, Pioneer Instrument Division, Bendix Aviation Corporation, Bendix, N. J.

Subcommittee on Medicine:

Lowell J. Reed, *Chairman.*

John W. Fertig, College of Physicians and Surgeons, Columbia University.

Hugo Muench, Rockefeller Foundation.

Margaret Merrell, School of Hygiene and Public Health, the Johns Hopkins University.

Alan E. Treloar, School of Medicine, University of Minnesota.

SCIENTIFIC NOTES AND NEWS

DR. RAY LYMAN WILBUR, chancellor of Stanford University, received on February 1 at the annual national dinner meeting of the American Social Hygiene Association, of which he is president, the William Freeman Snow Medal "for distinguished service to humanity." The medal was awarded "in recognition of the outstanding work he has done to protect American youth from the ravages of social disease."

DR. M. E. WEEKS and Jack Todd, of the Kentucky Agricultural Experiment Station, will receive the King Award for the most meritorious paper presented for 1942 by the Kentucky Academy of Science for their paper, "The Determination of Magnesium as the Quinolate Using the Colorimetric Ferric Chloride Method."

STANLEY FIELD has been reelected president of Field Museum of Natural History and has begun his thirty-fifth consecutive year of service in that office.

PROFESSOR W. D. CAIRNS, of Oberlin College, has been elected president of the Mathematical Association of America. Professor C. C. MacDuffee, of

Hunter College, has been elected *second vice-president;* Professors Saunders Mac Lane, of Harvard University, and E. J. Moulton, of Northwestern University, *governors at large,* and Professor B. W. Jones, of Cornell University, *associate secretary.* On January 1, Professor W. B. Carver, of Cornell University, became secretary-treasurer. The office of the association is now in McGraw Hall, Cornell University, Ithaca, N. Y.

THE New York City branch of the Society of American Bacteriologists has elected the following officers for the year 1943: *President,* Mary B. Horton; *Vice-president,* Gustav Steffen, and *Secretary-Treasurer,* Mortimer L. Starr, department of biology, Brooklyn College.

DR. MAYO H. SOLEY, associate professor of medicine and lecturer in pharmacology, has been made chairman of the division of pharmacology at the University of California Medical School, San Francisco. He has been appointed to succeed Dr. Chauncey D. Leake, who recently became dean of the Medical School at Galveston of the University of Texas.

DR. LEO S. MASON, head of the department of chemistry at the North Texas Agricultural College, has been appointed assistant professor of chemistry at the University of Pittsburgh and senior research fellow in physical chemistry. Dr. Bernard F. Daubert, assistant professor of chemistry on leave from the College of Pharmacy of the University of Pittsburgh, has been appointed senior fellow in biochemistry at the university.

THE National Research Council announces the appointment of Dr. Douglas M. Whitaker, of the department of biology of Stanford University, as executive secretary of the Division of Biology and Agriculture. Dr. Whitaker will aid in coordinating research in biology and agriculture in relation to the war effort.

DR. THORNE M. CARPENTER, acting director of the Nutrition Laboratory of the Carnegie Institution of Washington, Boston, has been appointed director of the laboratory.

DR. ALFRED E. EMERSON, professor in the department of zoology at the University of Chicago; Dr. Charles H. Seevers, head of the department of zoology at the Central Young Men's Christian Association College of Chicago, and Alex K. Wyatt, a specialist in moths and butterflies, have become honorary associates in entomology on the staff of Field Museum of Natural History.

FREDERICK D. RICHEY, of Ashville, Ohio, has been appointed a member of the Division of Cereal Crops and Diseases of the Bureau of Plant Industry, with headquarters at Knoxville, Tenn. He will act as coordinator for the regional corn improvement program in the South, and direct the state corn program cooperative between the Tennessee Agricultural Experiment Station and the U. S. Department of Agriculture.

DR. WILBERT MCLEOD CHAPMAN has resigned his position as director of the Washington State Shellfish Laboratory to become curator of fishes in the California Academy of Sciences, San Francisco.

DR. H. H. FOSTER, plant pathologist at the Tobacco Institute of Puerto Rico, has been appointed plant pathologist at the Truck Crops Experiment Station at Crystal Springs of the Mississippi Agricultural Experiment Station. George Y. Young, assistant plant pathologist of the Division of Cereal Crops and Diseases, Bureau of Plant Industry, has been transferred to the department of plant pathology at State College, Miss., where he will undertake investigations on diseases of corn.

BRYAN PATTERSON has been appointed curator of the division of paleontology at Field Museum of Natural History, Chicago. He has been acting curator since the retirement last year of Elmer S. Riggs, and had been previously assistant curator.

DR. ROBERT S. SHELTON has been promoted to the position of scientific director of the Wm. S. Merrell Company, pharmaceutical manufacturers of Cincinnati. He will be responsible for activities relating to research and product improvement. L. Dale Seif becomes chief chemist, and will have charge of all analytical and control work. Dr. L. V. Blubaugh has been made chief of the biological research and production departments.

DR. L. GRANT HECTOR, professor of physics at the University of Buffalo, has resigned to become director of engineering for the National Union Radio Corporation, of Newark, N. J.

DR. RICHARD S. UHRBROCK, head of the research department in the Industrial Relations Division of the Procter and Gamble Company, Cincinnati, has been appointed consultant in the training within industry program of the War Manpower Commission by Chairman Paul V. McNutt. He is developing a program for the selection of new supervisors in organizations holding war contracts.

PROFESSOR E. R. BECKER, of the department of zoology of Iowa State College, has been commissioned a captain in the Sanitary Corps of the U. S. Army.

DR. EUGENE W. SCOTT, research assistant at the Kettering Laboratory of Applied Physiology, Univer-

sity of Cincinnati, has been appointed gas officer in the Medical Division of the Office of Civilian Defense, Washington, D. C.

RICHARD F. FLINT, associate professor of geology at Yale University, an authority on glaciation, has leave of absence to accept a commission as a major in the Army Air Corps. He has been given an assignment concerned with the Arctic area with the Proving Ground Command of the Army Air Forces. His previous experience included work as senior scientist on the Byrd Expedition to Greenland in 1937, where he studied the glaciers and submarine connections between the Spitzbergen Islands and Greenland and journeyed within six hundred miles of the North Pole.

DR. HAMILTON SOUTHWORTH, assistant in medicine in the College of Physicians and Surgeons, Columbia University, has joined the staff of the Medical Division of the Office of Civilian Defense as a member of the Scientific Development and Research Section. Dr. Southworth will go to London shortly to represent the Medical Division as an intelligence officer. He has been commissioned in the U. S. Public Health Service in the grade of surgeon.

DR. FRANK E. EGLER, director of the Chicle Development Company Experiment Station and assistant professor on leave from the New York State College of Forestry, has been made senior dendrologist in the U. S. Forest Service, a war service appointment on the recently established Latin American Forest Resources Survey. He may be reached at the American Legation, San Jose, Costa Rica.

LLEWELYN WILLIAMS is leader of an expedition to make a survey in Peru in search of new supplies of cinchona bark.

DR. EUGENE L. OPIE, director of the department of pathology, Cornell University Medical College, New York, will deliver the second Edwin R. Kretschmer Memorial Lecture of the Institute of Medicine of Chicago on February 26. His subject will be "The Experimental Production of Leukemia and Its Significance in Relation to the Human Disease."

DR. WILLIAM J. ROBBINS, director of the New York Botanical Garden, will deliver the fifth Harvey Society lecture of the current series at the New York Academy of Medicine on February 18. Dr. Robbins will speak on "Some Internal Factors Limiting Growth."

LIEUTENANT COLONEL PAUL F. RUSSELL, U. S. Army, chief of the Tropical Disease and Malaria Control Section of the Division of Preventive Medicine, Office of the Surgeon General, Washington, D. C., will deliver the annual Hermann M. Biggs Memorial Lecture on April 1 at the New York Academy of Medicine. His subject will be "Malaria and Its Influence on World Health."

DR. ROBERT CUSHMAN MURPHY, of the American Museum of Natural History, gave on January 20 the Schiff Foundation Lecture at Cornell University, Ithaca. With the aid of kodachrome motion picture films, the speaker discussed the marine investigations of the Diesel schooner *Askoy* in the Pacific west of Colombia, during the first half of 1941, and also described many aspects of geographic and historic interest along the little known Chocó coast between southern Panama and northwestern Ecuador.

THE *Journal* of the American Medical Association reports that the Academia Nacional de Medicina of Buenos Aires has established the Hirsch Medical Scholarships with a fund of 500,000 pesos (about $125,000) given by Alfredo Hirsch of Buenos Aires. The work of these scholars will be carried out in the United States or in England for two years beginning by the middle of 1943. For the first ten years the scholarships will be given for studies on cancer, leprosy or infantile paralysis.

DISCUSSION

FURTHER COMPUTATIONS IN CHEMICAL PROGRESS

THE curve of chemical progress, based on the abstracts in *Chemical Abstracts,* and first published in SCIENCE for February 14, 1936, when prolonged to bring it up to date, shows important changes in slope. These changes in slope seem to indicate a close tying up of peaceful living with progress.

The full curve, shown in Fig. 1, like the curve published in 1936, is based wholly on the number of journal articles on chemistry indexed each year by the editors of *Chemical Abstracts.* Thus a little less than 8,000 journal articles were indexed in 1907, about 2,000 more the next year, and so on until 1913, when a little over 19,000 were indexed. Then the number dropped at a somewhat faster rate until 1918.

In 1919 the curve resumed its upward course at the old rate of a 2,000 increase each year, continuing, with two breaks which must be noted and explained, until a peak of almost 46,000 was reached in 1938, more than five times the rate of progress in 1907.

The curve turned completely in 1938 and plunged downward until it reached 31,000 (estimated in part) for 1942.

In other words, the present war has wiped out the growth of chemical progress during the last eight years, setting chemistry almost back to the year 1929.

Under the headline "Pure Science Held up by War," the *New York Sun,* October 21, 1942, explained how the Smithsonian Institution has turned away from its path of peaceful days when it "devoted itself to the furthering of fundamental knowledge, much of which has had little practical significance at the moment, but which has produced a secure foundation for practical development."

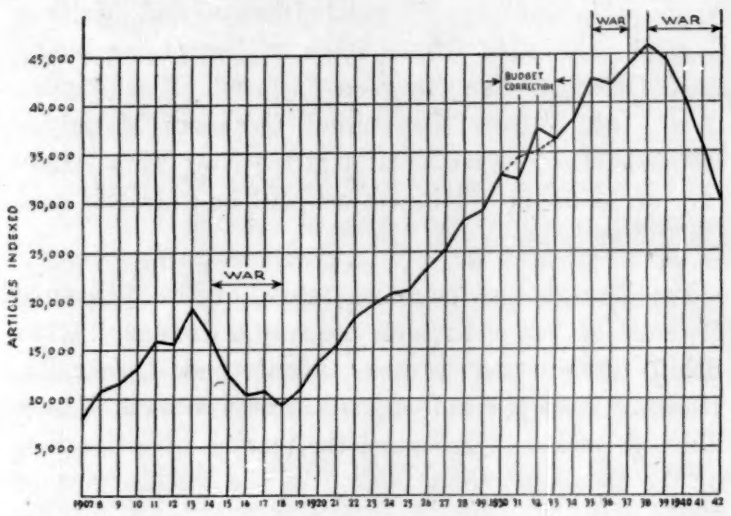

FIG. 1

During the war this work "must be temporarily suspended," and the staff of almost 100 scientists has been coordinated for the work of answering scientific inquiries sent in by the military, drawing the answers from "accumulated knowledge." Thus there have been no research results to publish from the Smithsonian Institution, to take it as one example of the effect of war on scientific progress.

The apparent drop at the year 1931 is apparent only. The budget makers mistakenly assumed that the financial depression, beginning in 1929, would begin to show in diminishing journal articles by 1931, and therefore they restricted the budget of the *Chemical Abstracts* editors in that year.

No such diminishing of journal articles appeared and 2,500 journal articles were held over from 1930 for indexing until 1931. The dotted line crossing 1930 makes this correction for the 2,500 held over so that the curve becomes practically straight until it drops slightly in 1936, the year Italy conquered Ethiopia.

Apparently the threatening war clouds of that year, 1936, adversely affected chemical progress nearly as much as the war clouds affected it in 1939.

One added phenomenon seems worth mentioning, and that is the parallelism between chemical progress and mechanical progress. The ratio of chemical patents to mechanical patents issued in the United States has not altered greatly in many years. For the last year, with wide fluctuations, the issue of chemical patents has averaged about 10 per cent. of all patents issued, as against 7 to 8 per cent. in the thirty years preceding 1936. The obvious inference is that war affects mechanical and chemical progress alike, and now seems to be adversely affecting mechanical progress a little more severely than it affects chemical progress.

To those who set up the theory that wartime progress is kept secret for some years and is published later the answer is that no such phenomenon can be deduced from the curve following the year 1919. The oft-repeated statement that war helps progress is true only in a few very narrow fields where industry learns to turn to hitherto unused sources of information, such as Smithsonian Institution, and profits by that information.

For the most part, research organizations, in wartime, are weakened or the experts are put on inspection work or are set to work in unfamiliar fields, so that less progress becomes possible.

JOURNAL ARTICLES ABSTRACTED ANNUALLY IN CHEMICAL ABSTRACTS

Year	Numbers of Abstracts	Year	Numbers of Abstracts
1907	7,975	1925	20,951
1908	10,835	1926	23,103
1909	11,455	1927	25,037
1910	13,006	1928	28,153
1911	15,892	1929	29,083
1912	15,740	1930	32,731
1913	19,025	1931	32,278
1914	16,468	1932	37,403
1915	12,290	1933	36,139
1916	10,519	1934	38,371
1917	10,921	1935	42,593
1918	9,283	1936	41,927
1919	10,957	1937	44,032
1920	13,619	1938	45,917
1921	15,211	1939	44,414
1922	18,070	1940	40,624
1923	19,507	1941	35,588
1924	20,523	1942	30,479

EDWARD THOMAS

WOOLWORTH BUILDING,
NEW YORK, N. Y.

SYNCHRONY IN FLOCK WHEELING

THE problem of the synchronization of action of cells and organisms has long attracted the interest of biologists. Separate units often respond with such simultaneity or under such other conditions that, in the case of neurones, ordinary conducted nerve impulses seem to be excluded.[1,2,3] Similarly with the behavior of organisms—insect flashes,[4] plant blooming, fish wheeling, and the like.[1,5]

[1] R. W. Gerard, *Scientific Monthly,* 44: 48–56, 1937.
[2] R. W. Gerard, *Ohio Jour. Science,* 41: 160–172, 1941.
[3] R. W. Gerard, *Annual Review of Physiology,* 4: 329–358, 1942.
[4] R. Ruedeman, SCIENCE, 86: 222–3, 1937. G. Alexander, SCIENCE, 82: 440–1, 1935. H. A. Allard, SCIENCE, 82: 517, 1935.

Some time ago an opportunity presented which enabled me to time the wheeling of a small bird flock with considerable precision. As I drove along a Vermont hilltop road at 35 miles per hour, the speed noted by chance just at the right time, a flock of something under half a hundred birds flew parallel to me not over fifteen feet from the car window and at precisely my speed. After a few seconds of this the flock wheeled away—not columns left, but each individual left face. I could not detect the slightest shift of position of one individual relative to the group. Surely none continued forward anything like its own length, perhaps 9 inches, after the others had turned.

Flying at 35 miles per hour, a bird lagging only ten milliseconds behind its fellows would have shot six inches ahead before making the turn. Clearly all the birds swerved simultaneously, within a maximum variation of less than five milliseconds.

What the cue or signal was which initiated the group maneuver, I do not know. No leader moved first and was followed by the others—I could not have failed to see the sequence. And any optic or even auditory stimulus, with a probable minimal reaction time of at least 100 milliseconds, must have acted with extreme constancy on the separate individuals. Even the Rockettes, elaborately trained to pretimed movements, can not approach such precision.

R. W. GERARD

DEPARTMENT OF PHYSIOLOGY,
UNIVERSITY OF CHICAGO

SCHOOLCRAFT AND THE AMERICAN ETHNOLOGICAL SOCIETY

IN recent issues of SCIENCE, there are some interesting articles about the American Ethnological Society in which Albert Gallatin has been mentioned as its founder. The centennial of this organization seems a proper time to consider the suggestion that Schoolcraft should be given at least joint credit for its establishment.

Schoolcraft had a genius for the construction of vehicles for scholarly activity, first manifested at the age of sixteen at Guilderland, N. Y., and afterwards wherever he went.

The last words in his first book, published in New York City in 1819, emphasized the need of a society for the study of antiquities in the United States ("A View of the Lead Mines of Missouri," p. 294).

In the spring of 1825, again while visiting in New York City, he, with Mr. Conant and Mr. Dwight, definitely arranged for a magazine devoted to Indian subjects, with Wilder and Campbell, publishers ("Memoirs," p. 207).

Disappointed in this, in December of the same year, at Sault Ste. Marie, Mich., Schoolcraft began a literary-ethnological magazine of his own, in manuscript, which circulated not only in that military outpost but considerably in the East as well.

In 1832, in Detroit, he organized the ethnological-humanitarian Algic Society, whose activities centered wherever he went and did not survive his interest.

Credit for establishment of the first common school journal in the United States, published in Michigan, 1838–1839, was originally given to John D. Pierce, then state superintendent of public instruction. It has now been shown that the launching influence in this was Schoolcraft, whose committee chose Mr. Pierce for editor and publisher because of the prestige of the latter's position as well as his ability.

The great Lewis Cass for years has been proudly claimed as founder of the Historical Society of Michigan. Now it has been made clear that, although deeply interested in scholarly matters, Governor Cass manifested no organizational urge for the better part of two decades of residence in Michigan; but that the Historical Society of Michigan sprang into being within a few weeks after Schoolcraft arrived in Detroit, in 1828, as a member of the Territorial Legislative Council. Schoolcraft secured for the organization its state charter and the potent name of Cass for its first president; and made all members of the legislative council members *ex officio* in order to give the society official countenance and secure a place of meeting for it.

Late in 1841 Schoolcraft left Michigan for New York City. The middle months of 1842 he spent in Europe, where he contacted and was particularly interested in scholarly organizations (manuscript paper, "Scientific Associations Abroad," in files of New-York Historical Society). On his return from Europe in 1842 he settled in New York City. Immediately the American Ethnological Society was founded—in November of that year.

The distinguished Albert Gallatin had been in New York City since 1828.

A contemporary biographical sketch of Schoolcraft, published unquestionably with his approval, says that "in 1841 he removed his residence from Michilimackinack to the city of New York, where he was instrumental, with Mr. John R. Bartlett, Mr. H. C. Murphy, Mr. Folsom and other ethnologists, in forming the American Ethnological Society—which, under the auspices of the late Mr. Albert Gallatin, has produced efficient labors" ("Memoirs," xlv).

It would appear that, in the case of the American Ethnological Society as so often, Schoolcraft again had hitched his vehicle for scholarship to a starry

[5] W. C. Allee, "Animal Aggregations," University of Chicago Press, 1931.

individuality, thereby conspicuously advancing scientific interests but obscuring his own all-important part in the procedure.

Full consideration might find it just henceforth to give Schoolcraft at least joint credit with Gallatin for the foundation of the American Ethnological Society.

CHASE S. OSBORN
STELLANOVA OSBORN
POSSUM POKE IN POSSUM LANE,
POULAN, WORTH COUNTY, GEORGIA

SPECIAL CORRESPONDENCE

WOUND HEALING

DR. S. PILIPCHUK, executive secretary of the Moscow Soviet Scientists Anti-Fascist Committee, has sent to SCIENCE the following communications by wireless from Moscow.

HEALING WOUNDS BY SKIN TRANSPLANTATION

Wound healing by the method of transplanting tissues evolved by Academician Filatov and his school is now widely practised. Particular attention has been attracted by the work of Professor Krause (Saratov) who has applied dead tissues chemically treated with chloraclyde in the healing of fresh and granulated wounds and chronic ulcers. Experience has shown that transplanted chloraclyde-treated tissues have the same, and in some cases even better, curative action. For grafting, Professor Krause has suggested using preserved skin from dead bodies and later chemically treated animal tissues, while his assistant Levkov uses the pericarpoidal [pericardial?] membrane treated the same way.

Hundreds of transplantations made in the Saratov Hospital on chronically non-healing ulcers, fistulas, burns, frostbite, skin diseases and in corneal lesions yielded excellent results in practically all instances. Surgical Clinic Pikin, candidate for the degree of doctor of medical sciences, has applied Professor Krause's method, using chemically treated pericarpoidal [?] skin from corpses and animal abdominal tissues. Careful preparation of transplanted skin is of the utmost importance. After being sprayed with chloraclyde solution the wound is drained, then sprayed again with chloraclyde. A piece of skin of the same form and shape as the wound, but slightly smaller than its surface area, is laid on the wound and fixed by several ligatures. This is covered by dry aseptic dressings. Pain in patched wounds ceases in from one to three hours after transplanting the skin. Healing takes less time under the grafted skin than in ordinary aseptic treatment. The bandage remains dry, and the scar remaining when the healing process is complete is small, soft and mobile.—N. EGOROV.

STIMULATION OF WOUND HEALING

Professor Goldberg, who holds the chair of pathological physiology in the Tomsk Medical Institute, suggests embryonal emulsion in the form of a liquid ointment made on a castor oil base for stimulation of the healing processes in wounds. Embryos are taken from guinea pigs, divided with scissors, and carefully ground with a small quantity of sterilized castor oil. Zeroform is added in the ratio of 0.3 parts to every 100 cc of oil. Tests made with this ointment on trophic ulcers in the Tomsk surgical clinics and hospitals prove that during the second phase of wound healing, and also when the process is sluggish, when granulation is either absent or poorly developed and there is sluggish regeneration of epithelium, this ointment has definite beneficial effect. This is frequently apparent after one or two dressings. It has an unquestionable stimulating influence on the regeneration of epithelium.—N. EGOROV.

MESSAGE RECEIVED BY THE AMERICAN ASSOCIATION OF SCIENTIFIC WORKERS FROM THE SOVIET SCIENTISTS ANTIFASCIST COMMITTEE

WE have received your letter of greetings through Professor Propper-Grastchenkov. Your proposal to establish closer contact between American and Russian scientists has met with greatest approval among Soviet men of science.

Soviet scientists are struggling for freedom and independence of all nations and for preservation of science and culture. . . .

In the struggle being waged by the democratic countries against fascist reaction science and technique play an important part. Soviet scientists spare no efforts in helping the Red Army to hasten the complete defeat of Hitlerism.

Several conferences were held in our country recently at which the work of scientists in wartime was discussed and plans for new efforts outlined. At the Jubilee Session of the Academy of Sciences of the USSR, convened in November, the results of scientific endeavor during the quarter century of Soviet power and the work of scientists in the war against Hitlerism were reviewed. Some time later there was a joint plenum of the medical councils of the People's Commissariat for Health of the USSR and of the Commissariat for Health of the RSFSR. The session of the Lenin All-Union Academy of Agricultural Sciences met in December.

At all these conferences a summary of what was done in each respective field of science was discussed and plans for further work in the war effort drawn up.

We believe that the exchange of reports on the

scientific activities of our freedom-loving countries would help to consolidate and widen our contacts. With this view in mind, we are in a position to despatch articles by Soviet scientists to American scientific journals.

Best New Year greetings to our American colleagues, wishing the American people success in hastening the defeat of Hitler's bands.

(Signed)

NIKOLAI DERZHAVIN,
President, Soviet Scientists Anti-fascist Committee
SERGEI PILIPCHUK,
Secretary

SCIENTIFIC BOOKS

THE "PIROTECHNIA" OF BIRINGUCCIO

The Pirotechnia of Vannoccio Biringuccio. Translated from the Italian with an introduction and notes by CYRIL STANLEY SMITH and MARTHA TEACH GNUDI. Publication sponsored by the Seeley W. Mudd Memorial Fund. xxviii + 476 pp. 92 illustrations. $7\frac{1}{2} \times 10\frac{1}{2}$ inches. New York: The American Institute of Mining and Metallurgical Engineers, 1942.

THE present century has witnessed an awakening of interest in several classic metallurgical treatises, as is indicated by the appearance of English translations of four important works of the sixteenth, seventeenth and eighteenth centuries. The first of these was the publication in 1912 by Herbert C. and Lou H. Hoover of their splendid translation of the first 1555 Latin edition of the "De Re Metallica" of Georgius Agricola. The second of these works was the translation in 1913 of "El Arte de los Metales" of Alvaro Alonso Barba by R. E. Douglass and E. P. Mathewson from the Spanish edition of 1640. The third of this group of treatises was the publication in mimeograph form in 1938 by the British Non-Ferrous Metals Research Association of the long-neglected translation by Arthur H. Searle of Emanuel Swedenborg's "Regnum Subterraneum, sive Minerale de Cupro et Orichalco" from the first Latin edition of 1734. The present English translation of the "Pirotechnia" of Biringuccio from the first Italian edition of 1540 is the fourth and latest member of this series of important historic metallurgical publications.

In the Introduction to the present edition of the "Pirotechnia" Dr. Gnudi gives first a two-page sketch of Biringuccio, who was born at Siena in 1480 and after a most adventurous life as a smelter and worker in metals died in 1538 or 1539. Dr. Smith then follows with a most interesting thirteen-page discussion of "The Background of the Pirotechnia and its Place in Metallurgical Literature" and of "The Editions of the Pirotechnia." The present edition, he remarks, "is the result of collaboration of two individuals whose chief fields of activity have been, respectively, in Italian literature and in metallurgy." Dr. Gnudi concludes the Introduction with two pages of remarks upon some of the problems encountered in making her translation.

The general scope of Biringuccio's "Pirotechnia" (by which was meant not so much pyrotechnics as pyrotechny in the broader sense of the use of fire in the mechanic arts) is indicated by the following brief synopsis of the ten books of the translation:

Book 1. Ores of gold, silver, copper, lead, tin, iron and making steel and brass.
Book 2. Ores of quicksilver, sulphur, antimony, vitriol, alum, arsenic and other so-called semiminerals.
Book 3. Assaying and preparing ores for smelting.
Book 4. Separation of gold from silver.
Book 5. Alloys of gold, silver, copper, lead and tin.
Book 6. Art of casting guns and objects of bronze such as bells.
Book 7. Methods of melting metals.
Book 8. Special methods of casting and moulding.
Book 9. Arts of alchemy, distilling, minting, metal working, extracting, etc. and of making wire, metallic mirrors, crucibles, pottery, lime and bricks.
Book 10. Manufacture of saltpeter, gunpowder, mines, bombs, etc. and fireworks for purposes of war and festivals.

To the ninety-nine strictly technical chapters, which make up the ten books of his Art of Fire, Biringuccio, for the sake of full measure, has added a final curious allegorical one hundredth chapter on the fire of love; "it consumes without leaving ashes, it is more powerful than all other fires, its smith is the great son of Venus, and its instruments, in place of glowing melting furnaces, bellows, hammers, and anvils, . . . are naught but quarrels, jealousies, fears and many other great and annoying agencies."

In addition to the flashes of wit and humor that appear here and in other pages of Biringuccio, the reader is impressed not only by the up-to-dateness of some of his descriptions of processes but also by the sagacity and common sense with which in an age of superstition he disposes of those who trust in divining rods, or in other magical devices, for locating mineral deposits, in the efficacy of which there are even now some believers. As for those who sought to produce precious metals by transmutation Biringuccio re-

marks: "I tell and advise you that I believe the best thing to do is to turn to the natural gold and silver that is extracted from ores rather than that of alchemy, which I believe not only does not exist but also, in truth, has never been seen by anyone, although many claim to have seen it." Similarly without arguing the matter he dismisses those who proclaimed the possibility of artificially creating human, or animal, or vegetable life by simply stating: "I cannot forbear saying that I do not believe them."

The present scholarly work of Drs. Smith and Gnudi will be all the more appreciated by both student and book collector for the reproduction of the title page of the first 1540 edition (interesting for its marginal engravings of apparatus) and for the eighty-four 2 × 4 inch reproductions of the original wood cuts of equipment and processes. In Appendix A are eight additional reproductions of drawings from Agricola and other authors to illustrate several of Biringuccio's descriptions. Appendix B gives an explanation of the weights and measures used by Biringuccio. Appendix C contains a list of the editions of the Pirotechnia. Appendix D is a bibliography of important metallurgical works with mention of English translations when such are known. An index of ten pages is also provided.

The typographic work of this edition, by Carl Purington Rollins at the printing office of the Yale University Press, is of the highest quality. As for the edition itself the reviewer can only repeat what Harvey S. Mudd, of the Seeley W. Mudd Memorial Fund Committee, has stated in his Foreword.

> Biringuccio's work is a classic and in its translation Dr. Smith and Dr. Gnudi have brought to bear the high degree of scholarship that it deserves. Dr. Gnudi made the translation at Dr. Smith's request and it was then refined "in the fire" of his scientific knowledge of the subject. The result is a book which the Institute is proud to place before its members and which the Memorial Fund Committee considers it a privilege to publish.

The book is one which should be read, and if possible owned, by all metallurgists and chemical technologists as well as by all students of the history of metallurgical arts.

C. A. BROWNE

CHEMISTRY

Introductory Chemistry for the Laboratory. By ALFRED BENJAMIN GARRETT, LAURENCE QUILL and FRANK HENRY VERHOEK. 239 pp. Ginn and Company. 1942. $1.60.

THIS manual contains 61 exercises, each of which will require two to four hours for performance and answering questions. The exercises are grouped into 14 units of related experiments, such as the gases of the air (Unit No. 1), acids (No. 3), the chlorine family (No. 6), compounds of sulfur, nitrogen, carbon (Nos. 9, 10, 11). An excellent unit is No. 12, raw materials for the inorganic chemical industries, which includes formation of useful compounds from natural carbonates, chlorides, sulfates, silicates and phosphates. Unit No. 13, metallurgy and reactions of some common metals, contains a few such interesting projects but consists mostly of test-tube reactions of metal salt solutions. Unit No. 14 consists of interesting applications of chemical principles—to water hardness, blueprinting, alloys, colloids, milk, butter, vinegar, baking powder, etc.

There is a wide choice of topics and ample opportunity for rearrangement for use with any text. There are a few quantitative experiments; this reviewer would prefer more. Appendixes I, II and III deal with fundamental techniques, weighing and elementary glass working, and since they are used immediately might well have been made into preliminary experiments. Most of the test-tube reactions are carried out on a semi-micro scale. An incongruity appears in the description of the "brown ring" test (p. 113) where five drops of nitrate and ferrous solutions are mixed in a small test-tube and five drops of concentrated sulfuric acid added; the accompanying diagram shows the acid being poured from a large wide-mouthed bottle.

The book is paper-bound, with the sheets perforated and punched for reassembling with rings. Each sheet has a blank for the student's name, and blanks are provided for answers to all questions. The printing is good, and there are few errors.

Semimicro Laboratory Exercises in General Chemistry. By J. AUSTIN BURROWS, PAUL ARTHUR and OTTO M. SMITH. xiii + 328 pp. The Macmillan Company. 1942. $2.50.

THIS laboratory manual is exceptionally well written, and the care, experience and interest of the authors in the student's progress are evident throughout. It introduces real semi-micro procedures from the start, with adequate directions, but does not hesitate to use small-scale macro-methods when this seems advisable. The saving in materials and time should be considerable, and the advantage of collecting 12 ml vials of dangerous or obnoxious gases instead of larger amounts is obvious. The experiments are thoroughly workable and most students should be stimulated by the careful but not at all difficult technique required.

The reviewer can do no better than to quote from the preface: "Balance has been maintained between descriptive experiments, quantitative experiments, experiments illustrating . . . laws and principles, and experiments illustrating applications of chemistry."

"The seventy-two exercises offer a wide variety of experiments from which the teacher . . . may choose a suitable number of almost any desired type." "Practical applications . . . are brought out here and there . . . to reveal to the student that chemistry is related to his personal existence." "More and more responsibility is thrown upon the student as he progresses from the earlier experiments to the later ones."

The description of materials and solutions required is complete and adequate. Each experiment has a set of "Preparatory Questions" for preliminary study, the "Procedure" with notes calling for observations to be written down and used as a guide in filling in blanks in the "Interpretation" pages, which are to be torn out and handed in. The whole book is paper-covered, with spiral binder, and all sheets are perforated and punched for reassembly with rings. The format is good, and there are few if any errors.

CECIL V. KING

SPECIAL ARTICLES

STUDIES ON THE ISOLATION OF THE FACTOR RESPONSIBLE FOR TISSUE INJURY IN INFLAMMATION[1, 2]

CAREFUL analysis of the various manifestations of inflammation reveals an essentially stereo-patterned reaction, irrespective of the causative irritant. The latter as well as the anatomical location of the lesion may influence the ultimate appearance of the inflamed area; but close scrutiny reveals the presence of a basic pattern.[3, 4, 5] This is characterized first by an increased fluid passage primarily referable to the liberation of leukotaxine. This substance as shown in earlier studies increases capillary permeability.[3] The alteration in the structure of the capillary endothelium allows the free passage of plasma proteins, including fibrinogen. The latter in the presence of injured tissue is precipitated as a fibrinous network.[3] The tributary lymphatics being evidently more delicate in structure than the capillaries are damaged at a relatively early stage, becoming thus occluded with fibrinous thrombi. The presence of coagulated plasma at the site of inflammation in addition to the occlusion of the tributary lymphatics induce, a lymphatic blockade which thus "walls-off" the inflammatory irritant. In this way inflammation as shown in a number of earlier studies plays an important rôle in immunity as a regulator of bacterial invasiveness.[6] Subsequently, polymorphonuclear leukocytes appear on the scene. Chemotaxis of these phagocytic cells is brought about by the liberation of leukotaxine.[3] Thus this substance is responsible for two of the basic sequences in the development of the inflammatory reaction, namely, increased capillary permeability and migration of polymorphonuclear leukocytes. The usual cytological sequence of polymorphonuclear leukocytes followed eventually by macrophages is conditioned by the local pH at the site of inflammation.[7] The developing local acidosis is in turn referable to a disturbance in the local intermediary carbohydrate metabolism.[8] The rise in number of circulating leukocytes is due to the liberation of a pseudo-globulin in the exudate. It has been termed the *leukocytosis-promoting factor*.[9] The interplay of the foregoing sequences ultimately disposes of the irritant and allows unhampered regeneration or repair.

In the last analysis the inflammatory reaction is a manifestation of severe cellular injury. Neither leukotaxine nor the leukocytosis-promoting factor induce the characteristic injury of inflammation. Besides the function ascribed above to these two substances, there is as a result of their presence in normal tissue scarcely any detectable cellular injury. An attempt has therefore been made now to identify the factor responsible for injury *per se*. Studies have been undertaken on the pleural exudates of dogs obtained as a result of turpentine injection. The results have been further substantiated by additional studies on exudative material obtained from man. In brief, it has been found that either dialysis of the exudate or its fractionation with usually one-third saturation of ammonium sulfate yields, after removal of the $SO^{=}_{4}$ by dialysis, a potent euglobulin fraction which rapidly induces severe tissue damage in rabbits and to some extent in dogs. The induced inflammatory reaction is characterized after a few hours not only by marked leukocytic infiltration but also by massive thrombosis both of lymphatics and to some extent of the small blood vessels. There is also present a fibrinous network in the tissue distended with edema. The presence of the elements inducing lymphatic blockade, which in themselves serve as a gauge of the degree of local injury, is fully substan-

[1] From the Department of Pathology, Harvard University Medical School, Boston, Massachusetts.

[2] Aided by a grant from the Jane Coffin Childs Fund for Medical Research and under a Government Contract from the Office of Scientific Research and Development.

[3] Valy Menkin, "Dynamics of Inflammation," Macmillan Company, New York, 1940.

[4] *Idem*, "Medico-Surgical Tributes to Harold Brunn," University of California Press, 1942, p. 275.

[5] *Idem*, *Physiol. Rev.*, 18: 366, 1938.

[6] *Idem*, *Am. Jour. Med. Sci.*, 190: 583, 1935.

[7] *Idem*, *Am. Jour. Path.*, 10: 193, 1934.

[8] Valy Menkin and C. R. Warner, *Am. Jour. Path.*, 13: 25, 1937.

[9] Valy Menkin, *Arch. Path.*, 30: 363, 1940.

tiated in numerous observations on rabbits. The introduction of trypan blue in an area of the axillary region, previously treated with the euglobulin fraction of exudate, is invariably followed by prompt local fixation of the dye as indicated by its inability to diffuse to the tributary lymphatic vessels and nodes. The introduction of the material in the cutaneous tissue of the abdomen of rabbits may or may not be accompanied by prompt local seepage of trypan blue previously injected intravenously; but in any case, contrary to leukotaxine, there is no diapedesis of leukocytes within the customary testing interval of approximately one hour. The collagenous material in such subcutaneous areas tends to be swollen and often appears somewhat ground-glass-like in appearance. The lymphatic blockade can be induced as early as about a half hour after the introduction of this protein substance. The material is thermolabile and non-diffusible. It can be dried by freezing in a Flosdorf-Mudd apparatus. The potency of the material is not appreciably reduced by the procedure. Some degree of fixation and manifest inflammation has been obtained following the injection of three milligrams of the desiccated material. The injection of this powerful substance obtained either from canine or human exudates is characterized, in the gross, in rabbits by intense redness, edema and frequent central necrosis. The tributary lymphatic nodes are usually erythematous and congested. The acute inflammatory reaction can not be elicited either by the pseudo-globulin (*i.e.*, the leukocytosis-promoting factor) or the albumin fraction of exudates derived from dogs or man. This fact, therefore, indicates that it is not the injection of foreign proteins into rabbits which is primarily responsible for the response. Furthermore, the effect can to a large extent be elicited by injecting the canine material into the cutaneous tissue of a dog. Finally, the acute reaction is not essentially referable to the insolubility of the euglobulin fraction, for it can be suspended as a very fine suspension in physiological saline. The injection of such a preparation elicits in the rabbit a similar effect accompanied by lymphatic blockade. As control for these findings similar fractions were obtained by treating the blood serum of dogs in precisely the same manner. It was found that fractionation or short-time dialysis of clear straw-colored serum yields a euglobulin fraction which, even though insoluble, is incapable of inducing in the rabbit a severe inflammatory reaction accompanied by lymphatic blockade. Trypan blue injected into such treated areas freely diffuses to the tributary lymphatics. Sera, however, containing large quantities of hemolyzed material or highly lipemic sera are apt to yield euglobulin fractions capable of inducing variable degrees of fixation of the dye. These facts suggest that the active fraction recovered from exudates is liberated from injured cells. Furthermore, it has been found that prolonged dialysis of serum for a period of thirty-six hours or over may give rise to an active euglobulin fraction. This is an interesting fact in view of the observation of Chick,[10] reported a number of years ago. This investigator pointed out that following prolonged dialysis a certain amount of pseudo-globulin is converted into euglobulin. One wonders whether such converted material may not be analogous to the injury factor or active euglobulin recovered from exudates. The active substance is absent in normal serum, but it can often be extracted from the blood serum of an animal with a concomitant acute inflammation. This fact points definitely to the significance of absorbed toxic material from the site of acute injury.

The foregoing facts demonstrate the presence of an injury factor in inflammatory exudates. This factor is found in the euglobulin fraction. It is therefore either a euglobulin or at least it seems to be associated with this protein fraction. The presence of such a chemical unit in exudative material warrants for the sake of convenience a name for this active biological substance. The term "necrosin" is therefore tentatively suggested. The untreated exudate *per se* induces when injected into rabbits a severe edematous inflammation characterized by lymphatic blockade. Fractionation of the exudate has yielded in the euglobulin fraction necrosin capable by itself of reproducing in an even more marked manner (undoubtedly due to the concentration and purification of the material) a similar picture as the whole exudate. The recovery of necrosin from exudates offers a reasonable explanation for the injury pattern revealed in an inflammatory reaction.[11]

The biological implications of this substance are at present being studied. The detail of this study as well as its effect on lymphatic blockade will be published *in extenso* elsewhere. In brief, necrosin injected into the circulation does not seem to alter appreciably the blood pressure of a cat. Intravenous administration of necrosin in a dog is followed by a marked leukopenia accompanied by transient toxic manifestations such as vomiting and diarrhea. Utilization of this finding has recently been employed in the further purification of the leukocytosis-promoting factor. By eliminating the euglobulin or necrosin, an active non-toxic leukocytosis-promoting factor is thus

[10] H. Chick, *Biochem. Jour.*, 8: 404, 1914.

[11] The basic pattern of injury in the development of various types of inflammation suggests that the irritant *per se* induces direct injury to the cell. The resulting deranged metabolism of the cell liberates various by-products (*e.g.*, leukotaxine, the leukocytosis-promoting factor, and necrosin) which act as common denominators in the development of a fundamentally basic pattern in inflammation.

obtained. It is conceivable that the presence or liberation of necrosin will explain, in part at least, the leukopenia frequently accompanying inflammatory processes. Finally, necrosin hastens markedly the rate of coagulation of blood *in vitro*. Whether this fact is due to thrombokinase associated with necrosin in the latter's present state of purification remains to be seen. Repeated injections of necrosin subcutaneously into rabbits induce the formation of precipitin antibodies to this substance. The implication of this finding remains to be determined.

In conclusion, the demonstration of an injury factor in the exudates of dogs and man, as brought down in the euglobulin fraction, and termed *necrosin* suggests further studies both in regard to the biological properties and the chemical purification of this substance. These investigations will form the subject of future communications.

VALY MENKIN

DEPARTMENT OF PATHOLOGY,
HARVARD UNIVERSITY MEDICAL SCHOOL

COLD AGGLUTININS (AUTOHEMAGGLUTININS) IN PRIMARY ATYPICAL PNEUMONIAS[1]

THREE cases have been encountered recently in which acute hemolytic anemia occurred in patients with the prevalent type of primary atypical pneumonia of unknown etiology. In two of these patients, difficulties in determining the blood group led to the discovery of a reversible autohemagglutinin (cold agglutinin). In certain other cases phlebothromboses and pulmonary emboli occurred during the latter part of the illness or during convalescence. Further study revealed that the great majority of the patients with primary atypical pneumonia tested this season showed cold agglutinins in dilutions of serum or plasma ranging from 1:10 to over 1:10,000 at 0° C.

This preliminary report is made because of the possibility that the development of cold agglutinins may serve as a criterion for segregating some of the prevalent cases of primary atypical pneumonia until definite etiological agents are established. The mechanism producing the autohemagglutinins is not known.

The maximum titer of cold agglutinins (in most cases 1:160 or 1:320 at 0° C.) was usually obtained at or near the end of the febrile period, and a rapid decline in titer occurred during convalescence. High titers were usually but not always obtained in the clinically severest cases. Essentially the same titers were obtained in serum from clotted blood and in plasma from oxalated samples. No hemagglutination was noted when the same samples were examined at 37° C. and the titer of cold agglutinins (tested at 0° C.) was unaffected by adsorption at 37° C. with erythrocytes of each of the four major blood groups.

A few of the patients in whom cold agglutinins were demonstrated also developed complement fixing antibodies for psittacosis and for the meningopneumonitis virus,[2] but these tests were negative in most instances.

A slight increase in the osmotic fragility of the erythrocytes was noted in some instances, but this was of a significant degree only in one of the patients who had acute hemolytic anemia. Tests were negative for autohemolysins, cold hemolysins (Donath-Landsteiner test), and the hemolysis test with acidified serum (Ham[3]).

Although the three patients with hemolytic anemia all had received sulfathiazole or sulfadiazine and many of the others in whom cold agglutinins were demonstrated were also treated with these drugs, a large percentage of those showing increased concentrations of autoagglutinins did not receive sulfonamide therapy throughout the course of their illness.

A number of samples of serum obtained from cases of primary atypical pneumonia of unknown etiology during the 1941–42 season failed to show cold agglutinins after six or more months of storage at 5° C. It is not known, however, whether or not this property was originally present in these samples or, as yet, whether the present sera will retain the property after 6 months under these conditions. Control sera obtained from cases of pneumococcus pneumonia and a variety of other febrile illnesses, most of them under treatment with sulfathiazole or sulfadiazine, were also examined for cold agglutinins with almost uniform absence of the agglutinins above a dilution of 1:4.

A brief review of the literature indicates that true reversible cold hemagglutinins have been demonstrated in significant titer only very rarely in cases of pneumonia. They have been noted in a few cases of various liver diseases or blood dyscrasias and, in a few instances, have been associated with peripheral vascular manifestations.[4,5] The only other infectious disease in which cold agglutinins have been found regularly is trypanosomiasis.[6]

OSLER L. PETERSON
THOMAS HALE HAM[7]
MAXWELL FINLAND

[1] From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

[2] These tests were carried out for us by Drs. Karl F. Meyer and Thomas Francis, Jr.

[3] T. H. Ham, *Arch. Int. Med.*, 64: 1271, 1939.

[4] R. P. McCoombs and J. S. McElroy, *Arch. Int. Med.*, 59: 107, 1937.

[5] K. M. Wheeler, H. J. Gallagher and C. A. Stuart, *Jour. Lab. and Clin. Med.*, 24: 1135, 1939.

[6] W. York, *Ann. Tropical Med. and Parasit.*, 4: 529, 1910.

[7] Aided, in part, by a grant from the John and Mary R. Markle Foundation.

SCIENTIFIC APPARATUS AND LABORATORY METHODS

PRODUCTION OF PANTOTHENIC ACID DEFICIENCY IN MICE WITH PANTOYL-TAURINE

MUCH evidence is accumulating to show that compounds with highly similar chemical configurations may interfere with each other with respect to their effects on living cells. The initial observations on the competitive relationships between sulfonamides and p-aminobenzoic acid in their effect on growth of microorganisms have been abundantly confirmed and extended by such reports as that of McIlwain,[1] who showed that pyridine-3-sulfonic acid and its amide interfere with nicotinic acid metabolism in microorganisms; and of Snell,[2] who showed that the physiologically inactive sulfonic acid N-(α, γ-dihydroxy-β, β-dimethylbutyryl)-turine (pantoyl-taurine[3]) interfered with the metabolism of pantothenic acid by lactic acid bacteria and yeast, apparently by blocking the essential pantothenic acid away from its site of action. No adverse effect of pantoyl-taurine on growth was observed if excess pantothenic acid were added simultaneously to the culture. McIlwain[3] has secured similar results with this substance on pathogenic bacteria. No data have been published concerning the effect of this substance on animals.

Pantoyl-taurine is relatively inactive on single oral or intraperitoneal administration to small mammals. No effects are noted from single doses as high as two grams per kilo of body weight in mice and rats. However, on long continued daily oral administration of pantoyl-taurine at a dose level of two hundred milligrams per kilo of body weight, evidence of pantothenic acid deficiency may be noted. After three to four weeks of such daily administration, growth in standard strains of laboratory mice ceased, the hair became roughened and porphyrin deposits appeared on the whiskers. There were also characteristic behavior symptoms similar to those observed in direct pantothenic acid deficiency.[4] These results were secured on a diet of Purina Fox Chow. This ration contains adequate pantothenic acid for mice in the absence of pantoyl-taurine. It thus appears probable that pantoyl-taurine interferes specifically with the metabolism of pantothenic acid in animals, as it does with microorganisms.

E. E. SNELL
L. CHAN
S. SPIRIDANOFF
E. L. WAY
C. D. LEAKE

UNIVERSITY OF TEXAS AND
UNIVERSITY OF CALIFORNIA,
SAN FRANCISCO

[1] H. McIlwain, *Brit. Jour. Exp. Path.*, 21: 136, 1940; *Nature*, 146: 653, 1940.
[2] E. E. Snell, *Jour. Biol. Chem.*, 141: 121, 1941.
[3] H. McIlwain, *Brit. Jour. Exp. Path.*, 23: 95, 1942.
[4] J. G. Sandza and L. R. Cerecedo, *Jour. Nutrition*, 21: 609, 1941.

A NEW FIXATIVE FOR ANIMAL TISSUES

A NEW general fixative, superior to any other so far tested, has been developed in connection with the routine toxicological work carried on in this laboratory. This solution not only fixes the tissues well, but it permits brilliant subsequent hematoxylin-eosin staining. It has the additional advantage of dehydrating the tissues as it fixes them.

Fixative:

Picric acid	5 parts
Isopropanol	55 "
Acetone	30 "
Acetic (glacial)	5 "
Formaldehyde (40 per cent. by vol. C.P.)	5 "

The length of fixation depends, as with other fixatives, on the size and nature of the tissues involved. From two hours to four days is recommended. Tissues have been left in this fixative for several days without apparent harm.

The tissues that are not imbedded in paraffin are stored in 70 per cent. isopropanol.

Since this solution fixes and dehydrates at the same time, it permits a direct transfer from the fixative to isopropanol. In general practice, tissues are trimmed and placed in the labeled cheesecloth "tea" bags in which they are transferred from one solution to another and through the paraffins until imbedded.

After fixation the tissues are washed in two changes of isopropanol (nearly absolute), one to two hours in each change. Then they are passed through three changes of dioxane, one to two hours in each change. The tissues are usually left overnight in the third change of dioxane. Infiltration is begun with two hours in a $\frac{1}{3}$ dioxane-$\frac{2}{3}$ paraffin mixture and completed in three changes of pure paraffin, one half to one hour for each, in a vacuum oven.

Tissues are sectioned from 4 to 7 microns thick. The picric acid is removed from the mounted sections with a 1.5 per cent. solution of ammonia hydroxide in 95 per cent. ethanol prior to staining.

M. ARDELLE CLEVERDON

STAMFORD RESEARCH LABORATORIES,
AMERICAN CYANAMID COMPANY

BOOKS RECEIVED

ANDREWS, ALBERT H. *Manual of Oxygen Therapy Techniques.* Pp. 191. The Year Book Publishers, Inc. $1.75.

BOWEN, E. J. *The Chemical Aspects of Light.* Illustrated. Pp. vi + 191. Oxford University Press. $4.00.

Carnegie Endowment for International Peace. Year Book, 1942. Pp. x + 152. Carnegie Endowment.

MABEE, CARLETON. *The American Leonardo, The Life of Samuel F. B. Morse.* Illustrated. Pp. xix + 420. Alfred A. Knopf, Inc. $5.00.

SCHUCHERT, CHARLES. *Stratigraphy of the Eastern and Central United States.* Illustrated. Pp. xvii + 1013. John Wiley. $15.00.

WEISS, EDWARD and O. SPURGEON ENGLISH. *Psychosomatic Medicine.* Pp. xxiii + 687. W. B. Saunders Company. $8.00.